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MEMORANDUM

To: Members of the Subcommittee on National Security, Emerging Threats, and International Relations

From: Christopher Shays
Chairman

Date: November 9, 2005

Subject: Briefing memo for November 15, 2005 Subcommittee hearing

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Attached find the briefing memo required by Committee rules for the hearing on Tuesday, November 15, 2005 entitled, *Examining VA Implementation of the Persian Gulf War Veterans Act of 1998.* The hearing will convene at 10:00 a.m. in room 2154 Rayburn House Office Building.

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MEMORANDUM

To: Members of the Subcommittee on National Security, Emerging Threats, and International Relations

From: Kristine K. Fiorentino KF

Subject: Briefing Memorandum for the hearing, *Examining VA Implementation of the Persian Gulf War Veterans Act of 1998,* scheduled for Tuesday, November 15, 2005, at 10 a.m. in Room 2154, Rayburn House Office Building.

PURPOSE OF THE HEARING

The purpose of the hearing is to discuss the implementation of the Persian Gulf War Veterans Act of 1998, specifically VA compliance with the statutory mandate to assess the extent and weight of data from animal studies in determinations of presumptive causality of disease not just as that data might suggest the plausibility of a biological mechanism.

HEARING ISSUES

1. **What is the status of the implementation of the Persian Gulf War Veterans Act of 1998?**

2. **To what extent have animal studies been used according to the law?**

BACKGROUND

In 1990, the Persian Gulf War brought together a number of international Coalition forces in response to Iraq's invasion of Kuwait. Iraq was suspected of possessing weapons of mass destruction (WMD), including nuclear, radiological, biological and chemical (NBC) weapons. Each nation in the Gulf War Coalition assessed the nature and extent of those threats and took a variety of defensive measures. Those included stockpiling and administering various drugs and vaccines, some of which were experimental.

Since the war's end in 1991, more than 125,000 U.S. veterans of the Gulf War have complained of illnesses. Typical complaints of Gulf War veterans are: flu-like symptoms, chronic fatigue, rashes, joint and muscle pain, headaches, memory loss, reproductive problems, depression, loss of concentration, and gastro-intestinal problems. Others suffer cancers, heart and lung problems, and amyotrophic lateral sclerosis (ALS) or Lou Gehrig's Disease.

Many believe they are suffering chronic disabling conditions as a result of wartime exposures to one or more of 33 toxic agents known to be present in the Gulf War theater of operations. Before, during and after the hostilities, U.S. troops were exposed to a variety of potentially hazardous substances. Potential exposures include chemical and biological warfare agents as well as pesticides, insect repellants, leaded diesel fuel, depleted uranium, oil well fires, infectious agents, the experimental drug pyridostigmine bromide (PB), and multiple vaccines including anthrax.

Exposures to WMD, along with defense measures against such exposures, have been evaluated by some researchers as possible causes of

thousands of illnesses among United States (U.S.) and United Kingdom (U.K.) forces.

Persian Gulf War Veterans Act of 1998

In 1998, Congressman Shays and 213 bipartisan co-sponsors introduced *The Persian Gulf War Veterans Health Act of 1998* (H.R. 4036). The bill would establish in law the presumption of service-connection for illnesses associated with exposure to toxins present in the war theatre. The VA Secretary would be required to accept the findings of an independent scientific body as to the illnesses linked with actual and presumed toxic exposures. **(Attachment 1, p. 1)** A similar bill, H.R. 4328, was included in the 1998 omnibus appropriations bill (under Title XVI-*Service Connection for Persian Gulf War Illnesses*, Division C, Sections 1601 & 1602), and enacted in October, Public Law 105-277. This section was entitled the *Persian Gulf War Veterans Act of 1998.* **(Attachment 2, p. 1)**

The *Persian Gulf War Veterans Act of 1998* states:

> (b)(1)(A) Whenever the [Department of Veterans Affairs] Secretary makes a determination described in subparagraph (B) the Secretary shall prescribe regulations providing that a presumption of service connection is warranted for the illness covered by that determination for purposes of this section. (B) A determination referred to in subparagraph (A) is a determination based on sound medical and scientific evidence that a positive association exists between- (i) the exposure of humans **or animals** to a biological, chemical, or other toxic agent, environmental or wartime hazard, or preventative medicine or vaccine known or presumed to be associated with service in the Southwest Asia theater of operations during the Persian Gulf War; and (ii) the occurrence of a diagnosed or undiagnosed illness in humans **or animals**. (2)(A) In making determinations for purposes of paragraph (1), the Secretary shall take into account-(i) the reports submitted to the Secretary by the National Academy of Sciences under section 1603 of the Persian Gulf War Veterans Act of 1998; and (ii)all other sound medical and scientific information and analyses available to the Secretary. (B) In evaluating any report, information, or analysis for purposes of making such

> determinations, the Secretary shall take into consideration whether the results are statistically significant, are capable of replication, and withstand peer review. (3) An association between the occurrence of an illness in humans **or animals** and exposure to an agent, hazard or medicine or vaccine shall be considered to be positive for purposes of this subsection if the credible evidence for the association is equal to or outweighs the credible evidence against the association. **(Attachment 2, p. 2)** *(emphasis added)*

Section 1603 of the *Persian Gulf War Veterans Act of 1998* provides, "for the National Academy of Sciences, an independent nonprofit scientific organization with appropriate expertise, to review and evaluate the available scientific evidence regarding associations between illnesses and exposure to toxic agents, environmental or wartime hazards or preventative medicine or vaccines associated with Gulf War service." **(Attachment 2, p. 4)**

The law states:

> For each agent, hazard or medicine or vaccine and illness identified under subsection (c), the National Academy of Sciences shall determine, to the extent that available scientific data permit meaningful determinations- (A) whether a statistical association exists between exposure to the agent, hazard or medicine or vaccine and the illness, taking into account the strength of the scientific evidence and the appropriateness of the scientific methodology used to detect the association; (B) the increased risk of the illness among human **or animal populations** exposed to the agent, hazard, or medicine or vaccine; and (C) whether a plausible biological mechanism or other evidence of a casual relationship exists between exposure to the agent, hazard, or medicine or vaccine and the illness. **(Attachment 2, p. 5-6)** *(emphasis added)*

Institute of Medicine (IOM) Gulf War and Health Series

In accordance with the *Persian Gulf War Veterans Act of 1998*, the Institute of Medicine (IOM) began reviewing the scientific and medical literature on the potential health effects of chemical and biological agents

related to the 1991 Gulf War. The first study entitled, *Gulf War and Health, Volume 1: Depleted Uranium, Pyridostigmine Bromide, Sarin, Vaccines* was published in 2000 and it examined the scientific literature on depleted uranium, chemical warfare agents (sarin and cyclosarin), pyridostigmine bromide and vaccines (anthrax and botulinum toxoid.) The second IOM study was published in 2003 and was entitled *Gulf War and Health Volume 2: Insecticides and Solvents.* The third IOM study was published in 2005 and was entitled *Gulf War and Health Volume 3: Fuels, Combustion Products and Propellants.* **(Web Resource 1)**

The IOM used the following categories of evidence in *Gulf War and Health Volume 1:*

- *Sufficient Evidence of a Casual Relationship.* Evidence is sufficient to conclude that a casual relationship exists between the exposure to a specific agent and a health outcome in humans. The evidence fulfills the criteria for sufficient evidence of an association (below) and satisfies several of the criteria used to assess causality: strength of association-dose response relationship, consistency of association, temporal relationship, specificity of association and biological plausibility.

- *Sufficient Evidence of and Association.* Evidence is sufficient to conclude that there is a positive association. That is, a positive association has been observed between an exposure to a specific agent and a health outcome in human studies in which chance, bias, and confounding could be ruled out with reasonable confidence.

- *Limited/Suggestive Evidence of an Association.* Evidence is suggestive of an association between exposure to a specific agent and a health outcome in humans, but is limited because chance, bias, and confounding could not be ruled out with confidence.

- *Inadequate/Insufficient Evidence to Determine Whether an Association Does or Does Not Exist.* The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an association between and exposure to a specific agent and a health outcome in humans.

- *Limited/Suggestive Evidence of No Association.* There are several adequate studies covering the full range of levels of exposure that humans are known to encounter that are mutually consistent in *not* showing a positive association between exposure to a specific agent and a health outcome at any level of exposure. A conclusion, of no association is inevitably limited to the conditions, levels of exposure, and length of observation covered by the available studies. In addition, the possibility of a very small elevation in risk at the levels of exposure studied can never be excluded. **(Web Resource 1, pp. 4-5)**

  According to the IOM:

  > These five categories describe different strengths of association, with the highest level being sufficient evidence of a casual relationship between exposure to a specific agent and a health outcome. The criteria for each category sound a recurring theme: An association is more likely to be valid to the extent that the authors reduced common sources of error in making inferences-chance variation, bias in forming a study chohort and confounding. Accordingly, the criteria for each category express varying degrees of confidence based upon the extent to which it has been possible to exclude these sources of error. **(Web Resource 1, p. 5)**

On January 24, 2003, Department of Veterans Affairs (VA) Secretary Anthony J. Principi, requested the Institute of Medicine examine the medical and scientific literature on the health effects of Sarin published since the 2000 IOM Report. In particular Secretary Principi requested recent studies regarding the effects of sarin on laboratory animals be examined to determine possible health consequences of human exposures. **(Attachment 3, p. 1)** The *Updated Literature Review of Sarin* was published on August 20, 2004. The results of the updated study were the same as the results of the initial review.

The report found sufficient evidence of a causal relationship between

- **Exposure to sarin and dose-dependent acute cholinergic syndrome that is evident seconds to hours subsequent to sarin exposure and resolves in days to months.** It has been known for

several years exposure to sarin can cause a variety of signs and symptoms affecting the peripheral and central nervous systems. These signs are apparent seconds to hours after exposure and resolve over time.

The report found limited/suggestive evidence of an association between

- **Exposure to sarin at doses sufficient to cause acute cholinergic signs and symptoms and a variety of subsequent long-term neurological effects.** Several health effects are reported in the literature to persist after sarin exposure such as fatigue, headache, visual problems and symptoms of PTSD.

The IOM found inadequate/insufficient evidence to determine whether an association exists between

- **Exposure to sarin at low doses insufficient to cause acute cholinergic signs and symptoms and subsequent long-term adverse neurological health effects.** Due to the lack of human studies showing sarin or cyclosarin's long term health effects at doses that do not produce acute symptoms, the IOM decided the evidence was inadequate to determine if these effects exist.

- **Exposure to sarin and subsequent long-term cardiovascular effects.** The IOM found studies of the cardiovascular effects after sarin exposure inconsistent. **(Web Resource 1, pp. 9-11)**

Research Advisory Committee (RAC)

The Research Advisory Committee on Gulf War Veterans' Illnesses (RACGWVI) was appointed by the Department of Veterans Affairs Secretary Anthony J. Principi on January 23, 2002, pursuant to Public law 105-368. The mission of the Committee is to, "make recommendations to the Secretary of Veterans Affairs on government research relating to the health consequences of military service in the Southwest Asia theater of operations during the Persian Gulf War." **(Web Resource 2)** The Committee is tasked with reviewing all relevant research, proposed federal research plans, initiatives, procurements and other activities in support of research projects on Gulf War-associated illnesses.

Members of the Committee consist of the general public, Persian Gulf War veterans, representatives of veterans and members of the medical and scientific community. The Committee is required to meet at least twice a year and to submit an annual report on the status and results of government research during the previous year. **(Web Resource 2)**

DISCUSSION OF HEARING ISSUES

1. What is the status of the implementation of the Persian Gulf War Veterans Act of 1998?

Some would argue the *Persian Gulf War Veterans Act of 1998* has not been implemented as it was designed. The Department of Veterans Affairs contracted with the IOM to review the scientific literature on the potential health effects of agents Gulf War veterans may have been exposed to. However, according to the IOM, "Because only a few studies describe the veterans' exposures, the committee reviewed studies of any human population-including veterans-that had been exposed to the agent of concern at any dose. These studies come primarily from occupational, clinical, and healthy volunteer settings." **(Web Resource 1, p. 3)** Since it is difficult to compare human occupational settings with the exposures veterans faced in the Gulf War, some believe it would be better to rely on animal studies since an environment can be created similar to what Gulf War veterans experienced. However, animal studies were not used by the IOM to determine if an exposure caused a health outcome.

The IOM also notes the limitations of the scientific tools available in determining human health effects in the *Gulf War and Health Volume 3: Fuels Combustion Products, and Propellants* report:

> It should be noted that our available scientific tools-toxicology and epidemiology-are inadequate to illuminate clearly the human health effects of individual components of complex mixtures of the type experienced by Gulf War veterans. In many cases, the committee found 'inadequate/insufficient evidence of an association' between the exposure of concern and a health outcome; that may have been due to a lack of clear

evidence because of the inadequacy of those tools rather than to the absence of effects. **(Web Resource 1, p. 18)**

The *Persian Gulf War Veterans Act of 1998* states the VA Secretary should take into account the reports submitted by the IOM and "all other sound medical and scientific information and analyses available to the Secretary." **(Web Resource 1, p. 3)** However, some argue the Secretary has only used the IOM reports and has not taken into account other information. They argue the VA has used the findings from the IOM report to deny veterans' service connected benefits and have presented the IOM reports as scientific truth.

2. To what extent have animal studies been used according to the law?

The IOM did not use animal studies to determine if an exposure caused a health effect. Instead the IOM relied on human studies alone to make this determination. *Gulf War and Health Volume 1* states, "For its evaluation and categorization of the degree of association between each exposure and a human health effect, however, the committee only used evidence from human studies. Nevertheless, the committee did use nonhuman studies as the basis for judgments about biological plausibility, which is one of the criteria for establishing causation." **(Web Resource 1, p. 72)** Biological plausibility is "A causal association (or relationship between two factors) is consistent with existing medical knowledge." **(Web Resource 3)** According to the IOM, "Biological plausibility reflects knowledge of the biological mechanism by which an agent can lead to a health outcome." **(Web Resource 1, p. 80)**

However, the law does not limit the use of animal studies to biological plausibility. The law states, "An association between the occurrence of an illness in humans or animals and exposure to an agent, hazard or medicine or vaccine shall be considered to be positive for purposes of this subsection if the credible evidence for the association is equal to or outweighs the credible evidence against the association." **(Attachment 2, p. 2)**

The use of animal studies is important especially in terms of exposure to deadly agents such as sarin. Since it would be unethical and dangerous to

expose humans to sarin, researchers use animal studies to obtain information about potential health effects. Mice have similar immune function as humans and dogs have similar cardiovascular function as humans. Most of the medical advances we have today can be attributed to research in animals. **(Web Resource 4)** Thus, some question why the IOM did not look more carefully at animal studies when determining the association between exposures and health effects.

The IOM claims the category of evidence for association, "closely resemble those used by several IOM committees that evaluated vaccine safety, herbicides used in Vietnam, and indoor pollutants related to asthma." **(Web Resource 1, p. 4)** However, one key difference between the Agent Orange study and the Gulf War study is the IOM study limits the categories of associations to "health outcome in humans" **(Web Resource 1, p. 4)** while the Agent Orange study leaves it open to "health outcomes" thereby not eliminating health outcomes in animals. **(Web Resource 5, p. 7)**

Even when Department of Veterans Affairs (VA) Secretary Anthony J. Principi requested the Institute of Medicine update the literature review on sarin due to recent studies regarding the effects of sarin on laboratory animals, the IOM continued to limit the use of animal studies to biological plausibility alone.

The categories of association for the *Gulf War and Health: Updated Literature Review of Sarin* rely on health outcome in humans, not animals. The report states, "Animal studies had a small role in the committee's assessment of association between putative agents and health outcomes. In general, animal data were used for making assessments of biologic plausibility in support of the epidemiologic data rather than as part of the weight of evidence to determine the likelihood that an exposure to a specific agent might cause a long-term outcome." **(Web Resource 1, p. 2)** Some argue the animal data should be used to as part of the weight of evidence to determine the likelihood that an exposure to a specific agent may cause a long- term outcome. Since IOM did not use animal data in this way, some question the usefulness of updating the IOM report since the conclusions were the same as the ones contained in the original report.

Researchers who work with animal data find it hard to understand how the IOM can minimize relevant animal studies regarding health effects

from sarin exposure. They find it odd that the IOM would consider animal data inadequate or insufficient. The IOM report states:

> Data on experimental animals, especially from studies by Henderson et al. (2001, 2002), which were designed to mimic the potential exposures in the Gulf War, have demonstrated changes in muscarinic receptor density in specific brain areas. Those data are an important step in determining whether a biologically plausible mechanism could underlie any long-term effects of low exposure to chemical nerve agents, but more work needs to be conducted to elucidate potential mechanisms and clarify how the cellular effects are related to any clinical effects that might be seen. Therefore, in the absence of carefully designed human studies expressly of sarin's or cyclosarin's long-term health effects at doses that do not produce acute signs and symptoms, the committee concludes that the data remain inadequate or insufficient to determine whether persistent long-term effects are associated with low-level sarin exposure." **(Web Resource 1, p. 97)**

Even the Food and Drug Administration recognized the importance of animal studies when it finalized the Animal Efficacy Rule in May 2002. The Animal Efficacy Rule allows for the approval of certain new drugs and biological products for use in humans based on evidence of effectiveness derived solely from animal studies and any additional supporting data. **(Web Resource 6)**

It is not clearly understood why the IOM chose to limit the use of animal studies to judgments about biological plausibility. The law placed no such restriction on the IOM. Further questions need to be asked of IOM and VA in order to determine why animal studies were not considered as the law intended.

Mr. Mike Woods will testify about the illnesses he has experienced since serving in the Persian Gulf War.

Mr. Steve Robinson will testify about the status of Gulf War Illnesses research.

Mr. Jim Binns will testify about the work of the Research Advisory Committee on Gulf War Veterans Illnesses and concerns he has regarding the implementation of the *Persian Gulf War Veterans Act of 1998*.

Dr. Rogene Henderson will testify about the importance of using animal studies and data.

Dr. James P. O'Callaghan will testify about the importance of using animal studies and data.

Dr. Susan Mather will testify about how the Department of Veterans Affairs has complied with the *Persian Gulf War Veterans Act of 1998*.

Dr. Lynn Goldman will testify about the use of animal data and how the IOM has used it.

Dr. Sam Potolicchio will testify about his experience serving on three of the Gulf War studies including the sarin update.

ATTACHMENTS

1. H.R. 4036 "Persian Gulf War Veterans Health Act of 1998" June 11, 1998.

2. Public Law 105-277, Title XVI-Service Connection for Persian Gulf War Illnesses, "Persian Gulf War Veterans Act of 1998" October 21, 1998.

3. VA Secretary Anthony J. Principi letter to Dr. Harvey Fineberg, President of the IOM requesting an updated literature review of sarin due to recent studies regarding the effects of sarin on laboratory animals January 24, 2003.

4. Ms. Susanne Stoiber, Executive Director of the IOM, letter to Dr. Mark Brown, Director of the Environmental Agents Service at the VA regarding Secretary Principi's request for an update on health effects of sarin due to recent findings from animal studies.

5. Memorandum from Carolyn Fulco and Cathy Liverman, Study Directors at the IOM to Dr. Frances Murphy, at the VA regarding a progress report on the IOM Committee on Health Effects Associated with Exposures Experienced During the Persian Gulf War.

WEB RESOURCES

1. The Institute of Medicine Gulf War and Health Reports
   http://www.iom.edu/project.asp?id=4683

2. Research Advisory Committee On Gulf War Veterans' Illnesses
   http://www1.va.gov/rac-gwvi/

3. Definition of biological plausibility
   http://www.sabin.org/vaccine_science_GlossaryB_D.htm

4. Answers to key question about animal research
   http://www.faseb.org/opa/animal/animalpowerpt_files/Animal_Research_and_Disease.ppt

5. Veterans and Agent Orange Update 2004
   http://www.iom.edu/report.asp?id=25476

6. FDA News Release regarding Animal Efficacy Rule approval (May 30, 2002) http://www.fda.gov/bbs/topics/NEWS/2002/NEW00811.html

Committee on Government Reform
Subcommittee on National Security, Emerging Threats, and International Relations
"Examining VA Implementation of the Persian Gulf War Veterans Act of 1998"
(November 15, 2005)
Witness List

PANEL ONE

Mr. Mike Woods
Gulf War Veteran

Mr. Steve Robinson
Executive Director
National Gulf War Resource Center, Inc.

Mr. Jim Binns
Chairman
Research Advisory Committee on Gulf War Veterans Illnesses

Dr. Rogene Henderson
Senior Scientist
Lovelace Respiratory Research Institute

Dr. James P. O'Callaghan
Head
Molecular Neurotoxicology Laboratory
And CDC Distinguished Consultant
Toxicology and Molecular Biology Branch
Health Effects Laboratory Division
Centers for Disease Control and Prevention-NIOSH

PANEL TWO

Dr. Susan Mather
Chief Officer
Public Health & Environmental Hazards
Veterans Health Administration

Accompanied by:

Dr. Mark Brown
Director of the Environmental Agents Service
Department of Veterans Affairs

Mr. Richard J. Hipolit
Assistant General Counsel
Department of Veterans Affairs

Dr. Lynn Goldman
Professor of Occupational and Environmental Health
Department of Environmental Health Sciences
Johns Hopkins Bloomberg School of Public Health
Institute of Medicine

Dr. Sam Potolicchio
Professor of Neurology
Department of Neurology
The George Washington University Medical Center
Institute of Medicine

Susanne Stoiber
Executive Director
Institute of Medicine

Attachment 1

HR 4036 IH

105th CONGRESS

2d Session

H. R. 4036

To amend title 38, United States Code, to establish certain presumptions of service connection for veterans who served in the Persian Gulf War, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

June 11, 1998

Mr. SHAYS (for himself, Mr. TOWNS, Mr. SNOWBARGER, Mr. SANDERS, Mr. GILMAN, Ms. NORTON, Mr. BURTON of Indiana, Mr. METCALF, Mr. MCHUGH, Mr. ALLEN, Mr. LANTOS, Mr. BARRETT of Wisconsin, Mr. MCINTOSH, Ms. STABENOW, Mr. MCGOVERN, Mr. PAPPAS, Mr. SOUDER, Mr. WAXMAN, Mr. KUCINICH, Mr. KENNEDY of Massachusetts, Mr. DAVIS of Virginia, Mrs. JOHNSON of Connecticut, and Mr. UPTON) introduced the following bill; which was referred to the Committee on Veterans' Affairs

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A BILL

To amend title 38, United States Code, to establish certain presumptions of service connection for veterans who served in the Persian Gulf War, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the `Persian Gulf War Veterans Health Act of 1998'.

SEC. 2. PRESUMPTION OF SERVICE CONNECTION FOR ILLNESSES ASSOCIATED WITH SERVICE IN THE PERSIAN GULF DURING THE PERSIAN GULF WAR.

(a) IN GENERAL- (1) Subchapter II of chapter 11 of title 38, United States Code, is amended by adding at the end the following:

`Sec. 1118. Presumptions of service connection for illnesses associated with service in the Persian Gulf during the Persian Gulf War

`(a)(1) For purposes of section 1110 of this title, and subject to section 1113 of this title, each illness described in paragraph (2) or identified pursuant to subsection (b) shall be considered to have been incurred in or aggravated by service referred to in that paragraph, notwithstanding that there is no record of evidence of such illness during the period of such service.

`(2) An illness referred to in paragraph (1) is any diagnosed or undiagnosed illness that--

> `(A) the Secretary determines in regulations prescribed under this section to warrant a presumption of service connection by reason of having a positive association with exposure to a biological, chemical, or other toxic agent or environmental or wartime hazard known or presumed to be associated with service in the Armed Forces in the Southwest Asia theater of operations during the period beginning on August 2, 1990, and ending on December 31, 1991; and
>
> `(B) becomes manifest in a Persian Gulf War veteran who by reason of service in Southwest Asia during the period beginning on August 2, 1990, and ending on December 31, 1991, was exposed to such agent or hazard.

`(3) For purposes of this subsection, a Persian Gulf War veteran who has an illness described in paragraph (2) shall be presumed to have been exposed by reason of such service to the agent or hazard associated with the illness in the regulations prescribed under this subsection unless there is conclusive evidence to establish that the veteran was not exposed to the agent or hazard by reason of such service.

`(b)(1) The Secretary shall enter into a contract with an appropriate independent scientific body to establish a panel for the purpose of reviewing the medical and scientific literature to identify those diseases and illnesses epidemiologically, medically, or scientifically associated with exposure of humans or animals to any of the materials specified in subsection (c). The panel shall be composed of non-Government scientific experts representing, at minimum, the disciplines of toxicology, immunology, microbiology, molecular biology, genetics, biochemistry, chemistry, epidemiology, medicine, and public health.

`(2) The Secretary shall require that the panel submit to the Secretary, not later than one year after the date of the enactment of this section, a report, based upon the review under paragraph (1), identifying such diseases and illnesses.

`(3) Upon submission to the Secretary of the report under paragraph (2), each disease or illness identified in the report that becomes manifest in a Persian Gulf War veteran shall be presumed to be service-connected.

`(4) There is authorized to be appropriated to the Secretary $1,000,000 to carry out this subsection.

`(5) The specification of presumed exposures in subsection (c) shall be updated as information develops confirming the exposure of Persian Gulf War veterans or members of their families to additional chemical, biological, radiological, or other genotoxic or infectious materials. The Secretary shall periodically enter into a contract as described in paragraph (1) for the purposes of identifying and confirming such exposures. Upon submission to the Secretary of a report pursuant to such a contract, the Secretary shall add each disease or illness identified in the report that becomes manifest in a Persian Gulf War veteran to those diseases and illnesses that are presumed under this section to be service-connected.

`(c) PRESUMPTION OF EXPOSURE- Each Persian Gulf War veteran shall be presumed to have been exposed to the following potentially hazardous materials:

`(1) The following organophosphorous pesticides:

`(A) Chlorpyrifos.

`(B) Diazinon.

`(C) Dichlorvos.

`(D) Malathion.

`(2) The following carbamate pesticides:

`(A) Proxpur.

`(B) Carbaryl.

`(C) Methomyl.

`(3) The following carbamate used as nerve agent prophylaxis:

`(A) Pyridostigmine bromide.

`(4) The following chlorinated dydrocarbon and other pesticides and repellents:

`(A) Lindane.

`(B) Pyrethroids.

`(C) Rodenticides (bait).

`(D) Repellent (DEET).

`(5) The following low-level nerve agents and precursors compounds:

`(A) Sarin.

`(B) Tabun.

`(6) The following other synthetic chemical compounds:

`(A) Low-level mustard agents.

`(B) VOCs.

`(C) Hydrazine.

`(D) Red fuming nitric acid.

`(E) Solvents.

`(F) Uranium.

`(7) The following ionizing radiation:

`(A) Depleted uranium.

`(B) Microwave.

`(C) RF radiation.

`(8) The following environmental particulates and pollutants:

`(A) Hydrogen sulfide.

`(B) Oil fire byproducts.

`(C) Diesel heater fumes.

`(D) Sand micro-particles.

`(9) Diseases endemic to the region (including the following):

`(A) Leishmaniasis.

`(B) Sandfly fever.

`(C) Pathogenic escherechia coli.

`(D) Shigellosis.

`(E) Malaria.

`(10) Time compressed administration of multiple live, `attenuated,' and toxoid vaccines.

`(d) For purposes of this section:

`(1) The term `Persian Gulf War veteran' means a veteran who served on active duty in the Southwest Asia theater of operations during the period beginning on August 2, 1990, and ending on December 31, 1991.

`(2) The term `non-Government scientific expert' means an individual who is a scientific expert who (A) is not employed by the United States, and (B) received less than 15 percent of income during the preceding 12 months from federally funded research activities.'.

(2) The table of sections at the beginning of such chapter is amended by inserting after the item relating to section 1117 the following new item:

`1118. Presumptions of service connection for illnesses associated with service in the Persian Gulf during the Persian Gulf War.'.

(b) CONFORMING AMENDMENTS- Section 1113 of title 38, United States Code, is amended--

(1) by striking out `or 1117' each place it appears and inserting in lieu thereof `1117, or 1118'; and

(2) in subsection (a), by striking out `or 1116' and inserting in lieu thereof `, 1116, or 1118'.

SEC. 3. PLAN FOR MEDICAL SURVEILLANCE OF PERSIAN GULF WAR VETERANS AND THEIR FAMILIES.

(a) PLAN FOR CONTRACT TO ESTABLISH INDEPENDENT REVIEW PANEL- Not later than 180 days after the date of the enactment of this Act, the Secretary of Veterans Affairs shall submit to Congress a plan to contract with an appropriate independent scientific body to establish a panel, to be composed of non-Government scientific experts (as defined in section 1118(d)(2) of title 38, United States Code, as added by section 2), for the purpose of reviewing the statistical occurrence of both diagnosed and undiagnosed illnesses and symptoms among veterans of the Persian Gulf War and their families.

(b) CRITERIA AND PLAN FOR REVIEW- The criteria and a plan for such review shall be established by the panel and shall be submitted by the panel to the Secretary of Veterans Affairs and the chairman and ranking minority party member of the Committees on Veterans' Affairs of the Senate and the House of Representatives.

SEC. 4. PLAN FOR PERMANENT EXPERT ADVISORY GROUP ON CHEMICAL, BIOLOGICAL, AND RADIOLOGICAL DEFENSE.

Not later than 180 days after the date of the enactment of this Act, the President shall submit to Congress a plan for the establishment of a permanent expert advisory group to be composed of individuals capable of providing expert advice both to the President and the congressional defense and intelligence committees on the adequacy of current United States chemical, biological, and radiological defense technologies, procurement practices, and doctrine to defend the Armed Forces against both the immediate and chronic consequences of acute and sub-acute exposures to chemical, biological, radiological, or other genotoxic battlefield materials.

END

Attachment 2

(1) Paragraph (1) of section 9510(c) of the 1986 Code is amended to read as follows: 26 USC 9510.

"(1) IN GENERAL.—Amounts in the Vaccine Injury Compensation Trust Fund shall be available, as provided in appropriation Acts, only for—

"(A) the payment of compensation under subtitle 2 of title XXI of the Public Health Service Act (as in effect on August 6, 1997) for vaccine-related injury or death with respect to any vaccine—

"(i) which is administered after September 30, 1988, and

"(ii) which is a taxable vaccine (as defined in section 4132(a)(1)) at the time the vaccine was administered, or

"(B) the payment of all expenses of administration incurred by the Federal Government in administering such subtitle.".

(2) Section 9510(b) of the 1986 Code is amended by adding at the end the following new paragraph:

"(3) LIMITATION ON TRANSFERS TO VACCINE INJURY COMPENSATION TRUST FUND.—No amount may be appropriated to the Vaccine Injury Compensation Trust Fund on and after the date of any expenditure from the Trust Fund which is not permitted by this section. The determination of whether an expenditure is so permitted shall be made without regard to—

"(A) any provision of law which is not contained or referenced in this title or in a revenue Act, and

"(B) whether such provision of law is a subsequently enacted provision or directly or indirectly seeks to waive the application of this paragraph.".

(b) EFFECTIVE DATE.—The amendments made by this section shall take effect as if included in the provisions of the Taxpayer Relief Act of 1997 to which they relate. 26 USC 9510 note.

TITLE XVI—SERVICE CONNECTION FOR PERSIAN GULF WAR ILLNESSES

Persian Gulf War Veterans Act of 1998.

SEC. 1601. SHORT TITLE.

38 USC 101 note.

This title may be cited as the "Persian Gulf War Veterans Act of 1998".

SEC. 1602. PRESUMPTION OF SERVICE CONNECTION FOR ILLNESSES ASSOCIATED WITH SERVICE IN THE PERSIAN GULF DURING THE PERSIAN GULF WAR.

(a) IN GENERAL.—(1) Subchapter II of chapter 11 of title 38, United States Code, is amended by adding at the end the following:

"§ 1118. Presumptions of service connection for illnesses associated with service in the Persian Gulf during the Persian Gulf War

"(a)(1) For purposes of section 1110 of this title, and subject to section 1113 of this title, each illness, if any, described in paragraph (2) shall be considered to have been incurred in or aggravated by service referred to in that paragraph, notwithstanding that there is no record of evidence of such illness during the period of such service.

"(2) An illness referred to in paragraph (1) is any diagnosed or undiagnosed illness that—

Regulations.

"(A) the Secretary determines in regulations prescribed under this section to warrant a presumption of service connection by reason of having a positive association with exposure to a biological, chemical, or other toxic agent, environmental or wartime hazard, or preventive medicine or vaccine known or presumed to be associated with service in the Armed Forces in the Southwest Asia theater of operations during the Persian Gulf War; and

"(B) becomes manifest within the period, if any, prescribed in such regulations in a veteran who served on active duty in that theater of operations during that war and by reason of such service was exposed to such agent, hazard, or medicine or vaccine.

"(3) For purposes of this subsection, a veteran who served on active duty in the Southwest Asia theater of operations during the Persian Gulf War and has an illness described in paragraph (2) shall be presumed to have been exposed by reason of such service to the agent, hazard, or medicine or vaccine associated with the illness in the regulations prescribed under this section unless there is conclusive evidence to establish that the veteran was not exposed to the agent, hazard, or medicine or vaccine by reason of such service.

Regulations.

"(b)(1)(A) Whenever the Secretary makes a determination described in subparagraph (B), the Secretary shall prescribe regulations providing that a presumption of service connection is warranted for the illness covered by that determination for purposes of this section.

"(B) A determination referred to in subparagraph (A) is a determination based on sound medical and scientific evidence that a positive association exists between—

"(i) the exposure of humans or animals to a biological, chemical, or other toxic agent, environmental or wartime hazard, or preventive medicine or vaccine known or presumed to be associated with service in the Southwest Asia theater of operations during the Persian Gulf War; and

"(ii) the occurrence of a diagnosed or undiagnosed illness in humans or animals.

"(2)(A) In making determinations for purposes of paragraph (1), the Secretary shall take into account—

"(i) the reports submitted to the Secretary by the National Academy of Sciences under section 1603 of the Persian Gulf War Veterans Act of 1998; and

"(ii) all other sound medical and scientific information and analyses available to the Secretary.

"(B) In evaluating any report, information, or analysis for purposes of making such determinations, the Secretary shall take into consideration whether the results are statistically significant, are capable of replication, and withstand peer review.

"(3) An association between the occurrence of an illness in humans or animals and exposure to an agent, hazard, or medicine or vaccine shall be considered to be positive for purposes of this subsection if the credible evidence for the association is equal to or outweighs the credible evidence against the association.

"(c)(1) Not later than 60 days after the date on which the Secretary receives a report from the National Academy of Sciences

under section 1603 of the Persian Gulf War Veterans Act of 1998, the Secretary shall determine whether or not a presumption of service connection is warranted for each illness, if any, covered by the report.

"(2) If the Secretary determines under this subsection that a presumption of service connection is warranted, the Secretary shall, not later than 60 days after making the determination, issue proposed regulations setting forth the Secretary's determination. Regulations.

"(3)(A) If the Secretary determines under this subsection that a presumption of service connection is not warranted, the Secretary shall, not later than 60 days after making the determination, publish in the Federal Register a notice of the determination. The notice shall include an explanation of the scientific basis for the determination. Federal Register, publication.

"(B) If an illness already presumed to be service connected under this section is subject to a determination under subparagraph (A), the Secretary shall, not later than 60 days after publication of the notice under that subparagraph, issue proposed regulations removing the presumption of service connection for the illness. Regulations.

"(4) Not later than 90 days after the date on which the Secretary issues any proposed regulations under this subsection, the Secretary shall issue final regulations. Such regulations shall be effective on the date of issuance. Regulations. Effective date.

"(d) Whenever the presumption of service connection for an illness under this section is removed under subsection (c)—

"(1) a veteran who was awarded compensation for the illness on the basis of the presumption before the effective date of the removal of the presumption shall continue to be entitled to receive compensation on that basis; and

"(2) a survivor of a veteran who was awarded dependency and indemnity compensation for the death of a veteran resulting from the illness on the basis of the presumption before that date shall continue to be entitled to receive dependency and indemnity compensation on that basis.

"(e) Subsections (b) through (d) shall cease to be effective 10 years after the first day of the fiscal year in which the National Academy of Sciences submits to the Secretary the first report under section 1603 of the Persian Gulf War Veterans Act of 1998.". Termination date.

(2) The table of sections at the beginning of such chapter is amended by inserting after the item relating to section 1117 the following new item:

"1118. Presumptions of service connection for illnesses associated with service in the Persian Gulf during the Persian Gulf War.".

(b) CONFORMING AMENDMENTS.—Section 1113 of title 38, United States Code, is amended—

(1) by striking out "or 1117" each place it appears and inserting in lieu thereof "1117, or 1118"; and

(2) in subsection (a), by striking out "or 1116" and inserting in lieu thereof ", 1116, or 1118".

(c) COMPENSATION FOR UNDIAGNOSED GULF WAR ILLNESSES.—Section 1117 of title 38, United States Code, is amended—

(1) by redesignating subsections (c), (d), and (e) as subsections (d), (e), and (f), respectively; and

(2) by inserting after subsection (b) the following new subsection (c):

"(c)(1) Whenever the Secretary determines under section 1118(c) of this title that a presumption of service connection for an undiagnosed illness (or combination of undiagnosed illnesses) previously established under this section is no longer warranted—

"(A) a veteran who was awarded compensation under this section for such illness (or combination of illnesses) on the basis of the presumption shall continue to be entitled to receive compensation under this section on that basis; and

"(B) a survivor of a veteran who was awarded dependency and indemnity compensation for the death of a veteran resulting from the disease on the basis of the presumption before that date shall continue to be entitled to receive dependency and indemnity compensation on that basis.

Termination date.

"(2) This subsection shall cease to be effective 10 years after the first day of the fiscal year in which the National Academy of Sciences submits to the Secretary the first report under section 1603 of the Persian Gulf War Veterans Act of 1998.".

38 USC 1117 note.

SEC. 1603. AGREEMENT WITH NATIONAL ACADEMY OF SCIENCES.

(a) PURPOSE.—The purpose of this section is to provide for the National Academy of Sciences, an independent nonprofit scientific organization with appropriate expertise, to review and evaluate the available scientific evidence regarding associations between illnesses and exposure to toxic agents, environmental or wartime hazards, or preventive medicines or vaccines associated with Gulf War service.

(b) AGREEMENT.—The Secretary of Veterans Affairs shall seek to enter into an agreement with the National Academy of Sciences for the Academy to perform the activities covered by this section. The Secretary shall seek to enter into the agreement not later than two months after the date of enactment of this Act.

(c) IDENTIFICATION OF AGENTS AND ILLNESSES.—(1) Under the agreement under subsection (b), the National Academy of Sciences shall—

(A) identify the biological, chemical, or other toxic agents, environmental or wartime hazards, or preventive medicines or vaccines to which members of the Armed Forces who served in the Southwest Asia theater of operations during the Persian Gulf War may have been exposed by reason of such service; and

(B) identify the illnesses (including diagnosed illnesses and undiagnosed illnesses) that are manifest in such members.

(2) In identifying illnesses under paragraph (1)(B), the Academy shall review and summarize the relevant scientific evidence regarding illnesses among the members described in paragraph (1)(A) and among other appropriate populations of individuals, including mortality, symptoms, and adverse reproductive health outcomes among such members and individuals.

(d) INITIAL CONSIDERATION OF SPECIFIC AGENTS.—(1) In identifying under subsection (c) the agents, hazards, or preventive medicines or vaccines to which members of the Armed Forces may have been exposed for purposes of the first report under subsection (i), the National Academy of Sciences shall consider, within the first six months after the date of enactment of this Act, the following:

(A) The following organophosphorous pesticides:

(i) Chlorpyrifos.

(ii) Diazinon.
(iii) Dichlorvos.
(iv) Malathion.

(B) The following carbamate pesticides:
(i) Proxpur.
(ii) Carbaryl.
(iii) Methomyl.

(C) The carbamate pyridostigmine bromide used as nerve agent prophylaxis.

(D) The following chlorinated hydrocarbon and other pesticides and repellents:
(i) Lindane.
(ii) Pyrethrins.
(iii) Permethrins.
(iv) Rodenticides (bait).
(v) Repellent (DEET).

(E) The following low-level nerve agents and precursor compounds at exposure levels below those which produce immediately apparent incapacitating symptoms:
(i) Sarin.
(ii) Tabun.

(F) The following synthetic chemical compounds:
(i) Mustard agents at levels below those which cause immediate blistering.
(ii) Volatile organic compounds.
(iii) Hydrazine.
(iv) Red fuming nitric acid.
(v) Solvents.
(vi) Uranium.

(G) The following ionizing radiation:
(i) Depleted uranium.
(ii) Microwave radiation.
(iii) Radio frequency radiation.

(H) The following environmental particulates and pollutants:
(i) Hydrogen sulfide.
(ii) Oil fire byproducts.
(iii) Diesel heater fumes.
(iv) Sand micro-particles.

(I) Diseases endemic to the region (including the following):
(i) Leishmaniasis.
(ii) Sandfly fever.
(iii) Pathogenic escherechia coli.
(iv) Shigellosis.

(J) Time compressed administration of multiple live, 'attenuated', and toxoid vaccines.

(2) The consideration of agents, hazards, and medicines and vaccines under paragraph (1) shall not preclude the Academy from identifying other agents, hazards, or medicines or vaccines to which members of the Armed Forces may have been exposed for purposes of any report under subsection (i).

(3) Not later than six months after the date of enactment of this Act, the Academy shall submit to the designated congressional committees a report specifying the agents, hazards, and medicines and vaccines considered under paragraph (1). Reports.

(e) DETERMINATIONS OF ASSOCIATIONS BETWEEN AGENTS AND ILLNESSES.—(1) For each agent, hazard, or medicine or vaccine

and illness identified under subsection (c), the National Academy of Sciences shall determine, to the extent that available scientific data permit meaningful determinations—

(A) whether a statistical association exists between exposure to the agent, hazard, or medicine or vaccine and the illness, taking into account the strength of the scientific evidence and the appropriateness of the scientific methodology used to detect the association;

(B) the increased risk of the illness among human or animal populations exposed to the agent, hazard, or medicine or vaccine; and

(C) whether a plausible biological mechanism or other evidence of a causal relationship exists between exposure to the agent, hazard, or medicine or vaccine and the illness.

(2) The Academy shall include in its reports under subsection (i) a full discussion of the scientific evidence and reasoning that led to its conclusions under this subsection.

(f) REVIEW OF POTENTIAL TREATMENT MODELS FOR CERTAIN ILLNESSES.—Under the agreement under subsection (b), the National Academy of Sciences shall separately review, for each chronic undiagnosed illness identified under subsection (c)(1)(B) and for any other chronic illness that the Academy determines to warrant such review, the available scientific data in order to identify empirically valid models of treatment for such illnesses which employ successful treatment modalities for populations with similar symptoms.

(g) RECOMMENDATIONS FOR ADDITIONAL SCIENTIFIC STUDIES.—(1) Under the agreement under subsection (b), the National Academy of Sciences shall make any recommendations that it considers appropriate for additional scientific studies (including studies relating to treatment models) to resolve areas of continuing scientific uncertainty relating to the health consequences of exposure to toxic agents, environmental or wartime hazards, or preventive medicines or vaccines associated with Gulf War service.

(2) In making recommendations for additional studies, the Academy shall consider the available scientific data, the value and relevance of the information that could result from such studies, and the cost and feasibility of carrying out such studies.

(h) SUBSEQUENT REVIEWS.—(1) Under the agreement under subsection (b), the National Academy of Sciences shall conduct on a periodic and ongoing basis additional reviews of the evidence and data relating to its activities under this section.

(2) As part of each review under this subsection, the Academy shall—

(A) conduct as comprehensive a review as is practicable of the evidence referred to in subsection (c) and the data referred to in subsections (e), (f), and (g) that became available since the last review of such evidence and data under this section; and

(B) make determinations under the subsections referred to in subparagraph (A) on the basis of the results of such review and all other reviews previously conducted for purposes of this section.

(i) REPORTS.—(1) Under the agreement under subsection (b), the National Academy of Sciences shall submit to the committees and officials referred to in paragraph (5) periodic written reports regarding the Academy's activities under the agreement.

(2) The first report under paragraph (1) shall be submitted not later than 18 months after the date of enactment of this Act. That report shall include—

(A) the determinations and discussion referred to in subsection (e);

(B) the results of the review of models of treatment under subsection (f); and

(C) any recommendations of the Academy under subsection (g).

(3) Reports shall be submitted under this subsection at least once every two years, as measured from the date of the report under paragraph (2).

(4) In any report under this subsection (other than the report under paragraph (2)), the Academy may specify an absence of meaningful developments in the scientific or medical community with respect to the activities of the Academy under this section during the 2-year period ending on the date of such report.

(5) Reports under this subsection shall be submitted to the following:

(A) The designated congressional committees.

(B) The Secretary of Veterans Affairs.

(C) The Secretary of Defense.

(j) SUNSET.—This section shall cease to be effective 10 years after the last day of the fiscal year in which the National Academy of Sciences submits the first report under subsection (i).

(k) ALTERNATIVE CONTRACT SCIENTIFIC ORGANIZATION.—(1) If the Secretary is unable within the time period set forth in subsection (b) to enter into an agreement with the National Academy of Sciences for the purposes of this section on terms acceptable to the Secretary, the Secretary shall seek to enter into an agreement for purposes of this section with another appropriate scientific organization that is not part of the Government, operates as a not-for-profit entity, and has expertise and objectivity comparable to that of the National Academy of Sciences.

(2) If the Secretary enters into an agreement with another organization under this subsection, any reference in this section and section 1118 of title 38, United States Code (as added by section 1602(a)), to the National Academy of Sciences shall be treated as a reference to such other organization.

SEC. 1604. REPEAL OF INCONSISTENT PROVISIONS OF LAW.

38 USC 1117 note.

In the event of the enactment, before, on, or after the date of the enactment of this Act, of section 101 of the Veterans Programs Enhancement Act of 1998, or any similar provision of law enacted during the second session of the 105th Congress requiring an agreement with the National Academy of Sciences regarding an evaluation of health consequences of service in Southwest Asia during the Persian Gulf War, such section 101 (or other provision of law) shall be treated as if never enacted, and shall have no force or effect.

SEC. 1605. DEFINITIONS.

38 USC 1117 note.

In this title:

(1) The term "toxic agent, environmental or wartime hazard, or preventive medicine or vaccine associated with Gulf War service" means a biological, chemical, or other toxic agent, environmental or wartime hazard, or preventive medicine or vaccine that is known or presumed to be associated with service

in the Armed Forces in the Southwest Asia theater of operations during the Persian Gulf War, whether such association arises as a result of single, repeated, or sustained exposure and whether such association arises through exposure singularly or in combination.

(2) The term "designated congressional committees" means the following:

(A) The Committees on Veterans' Affairs and Armed Services of the Senate.

(B) The Committees on Veterans' Affairs and National Security of the House of Representatives.

(3) The term "Persian Gulf War" has the meaning given that term in section 101(33) of title 38, United States Code.

TITLE XVII—GOVERNMENT PAPERWORK ELIMINATION ACT

Government Paperwork Elimination Act. 44 USC 3504 note.

SEC. 1701. SHORT TITLE.

This title may be cited as the "Government Paperwork Elimination Act".

SEC. 1702. AUTHORITY OF OMB TO PROVIDE FOR ACQUISITION AND USE OF ALTERNATIVE INFORMATION TECHNOLOGIES BY EXECUTIVE AGENCIES.

Section 3504(a)(1)(B)(vi) of title 44, United States Code, is amended to read as follows:

"(vi) the acquisition and use of information technology, including alternative information technologies that provide for electronic submission, maintenance, or disclosure of information as a substitute for paper and for the use and acceptance of electronic signatures.".

SEC. 1703. PROCEDURES FOR USE AND ACCEPTANCE OF ELECTRONIC SIGNATURES BY EXECUTIVE AGENCIES.

(a) IN GENERAL.—In order to fulfill the responsibility to administer the functions assigned under chapter 35 of title 44, United States Code, the provisions of the Clinger-Cohen Act of 1996 (divisions D and E of Public Law 104–106) and the amendments made by that Act, and the provisions of this title, the Director of the Office of Management and Budget shall, in consultation with the National Telecommunications and Information Administration and not later than 18 months after the date of enactment of this Act, develop procedures for the use and acceptance of electronic signatures by Executive agencies.

(b) REQUIREMENTS FOR PROCEDURES.—(1) The procedures developed under subsection (a)—

(A) shall be compatible with standards and technology for electronic signatures that are generally used in commerce and industry and by State governments;

(B) may not inappropriately favor one industry or technology;

(C) shall ensure that electronic signatures are as reliable as is appropriate for the purpose in question and keep intact the information submitted;

(D) shall provide for the electronic acknowledgment of electronic forms that are successfully submitted; and

(E) shall, to the extent feasible and appropriate, require an Executive agency that anticipates receipt by electronic

Attachment 3

THE SECRETARY OF VETERANS AFFAIRS
WASHINGTON

January 24, 2003

Harvey Fineberg, M.D., Ph.D.
President
Institute of Medicine
The National Academies
500 Fifth Street, NW
Washington, DC 20001

Dear Dr. Fineberg:

The Department of Veterans Affairs appreciates and respects the excellent work contained in the Institute of Medicine (IOM) report on "Gulf War Health." As you know, this report was completed in 2000 in response to a Congressional requirement. The IOM, at that time, reviewed medical and scientific literature on the health effects of certain materials, including Sarin, that Gulf War veterans may have been exposed to during the 1991 Gulf War.

Recently, a number of new studies have been published on the effects of Sarin on laboratory animals. These studies have raised concerns with Gulf War veterans and other Americans regarding the relationship of these studies to possible health consequences of human exposures.

With this in mind, I am requesting IOM examine the medical and scientific literature on health effects of Sarin published since the 2000 Report. I ask that IOM report back to VA, as soon as possible, on whether this new research affects earlier conclusions of IOM. Specifically, in the interest of veterans' health, we would like to know if this new scientific information alters the conclusions about possible long-term health consequences of exposure to low levels of Sarin.

We look forward to meeting with you to discuss additional specifics and timing for this report. If you have any questions about this request, please contact Dr. Susan Mather, Chief Officer, Office of Public Health and Environmental Hazards, at (202) 273-8575.

Sincerely yours,

Anthony J. Principi

Attachment 4

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Susanne A. Stoiber
Executive Director

March 11, 2003

RE: NAS Proposal No. 03-IOM-051-01

Mark A. Brown, Ph.D.
Director
Environmental Agents Service (131)
Department of Veterans Affairs
810 Vermont Avenue, N.W.
Washington, DC 20420

Dear Dr. Brown:

We are pleased to submit the enclosed proposal, prepared by our Board on Health Promotion and Disease Prevention, in response to the Department of Veterans Affairs' (VA) request for an additional deliverable, Gulf War and Health: Updated Review of the Literature on Sarin, under Task Order #VA-2794-123. The total estimated cost of this project is $100,000.00 for the period from April 1, 2003 to October 31, 2003. As discussed with Institute of Medicine staff, there are sufficient funds remaining in the Gulf War and Health: Volume 2 budget to support this task. A no-cost extension has been requested to allow time to complete this task.

This proposal follows a request from Secretary Anthony J. Principi and discussions with yourself requesting an update of the health effects of the chemical warfare agent sarin; the original review of the health effects of sarin was part of Gulf War and Health: Volume 1. The request comes following the publication of new toxicology studies (three) showing effects in rats following exposure to chronic low doses of sarin and subsequent questions from veterans on whether those results would alter the conclusions of Gulf War and Health: Volume 1.

Commencement of this activity is subject to approval by the Executive Committee of the National Research Council Governing Board at its meeting on March 18, 2003.

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

500 Fifth Street, NW
Washington, DC 20001-2721

Phone: 202 334 2177
Fax: 202 334 1694
E-mail: sstoiber@nas.edu
www.iom.edu

The responsible staff officer for this study is Michelle Catlin, Ph.D., Senior Program Officer, 202-334-2777. She may be contacted regarding program matters. Business negotiations are the responsibility of Linda Kilroy, Contract Manager, Office of Contracts and Grants. She may be reached at 202-334-2428.

We shall appreciate your consideration of this matter.

Sincerely,

Susanne A. Stoiber

cc: Secretary Anthony J. Principi

Enclosures

Attachment 5

INSTITUTE OF MEDICINE
NATIONAL ACADEMY OF SCIENCES
2101 Constitution Avenue, Washington, D.C. 20418

Kathleen Stratton, Ph.D.
Director
Division of Health Promotion and Disease Prevention
fax: 202/334-2939

Committee on Health Effects Associated with
Exposures Experienced During the Persian Gulf War
Carolyn Fulco and Catharyn Liverman (study directors)
phone: 202/334-2039; email: pghealth@nas.edu

May 10, 1999

MEMORANDUM:

TO: Frances Murphy, M.D., MPH

FROM: Carolyn Fulco (CF) and Cathy Liverman (CL)

SUBJECT: Progress Report, IOM Committee on Health Effects Associated with Exposures Experienced During the Persian Gulf War

We are pleased to provide this progress report for the contract between the Department of Veterans Affairs (Contract Number V101 (93) p-1637, Task Order Number 1) and the Institute of Medicine.

As you know, the goal of this project is to conduct a review of the scientific and medical literature regarding adverse health effects associated with exposures experienced during the Persian Gulf War. The committee is reviewing the peer-reviewed literature on exposures related to Persian Gulf War Veterans when available, however, most of the literature is from environmental and occupational settings, as there is limited epidemiologic information in Persian Gulf Veterans. The IOM review will also include assessments of biologic plausibility and possible synergistic effects of combinations of exposures. The review will include recommendations for additional scientific studies to resolve areas of continued scientific uncertainty related to the health consequences of Gulf War service (statement of task enclosed).

The project is being conducted in three phases. The first phase will develop the methodology for conducting the study, select the first group of exposures, and review the literature for adverse health outcomes based on the selection of three to six exposures. Exposures may include, but are not limited to, depleted uranium, pesticides, insecticides, chemical and biological warfare agents, vaccines, pyridostigmine bromide (PB), heat stress, solvents, paints, fuels, smoke from oil-well fires, and sand. The second phase will review the remaining exposures and the final phase will be a series of updates of the literature, performed every two to three years. Because the data sources for assessing the relation between exposures and health effects vary greatly in quantity, quality, and applicability to the exposures experienced during the Gulf War, the review will include directions for future research to resolve continued scientific uncertainty.

To achieve those goals, the Institute of Medicine (IOM) immediately appointed staff to begin phase one of the project, following the award of the VA contract to the Institute of Medicine in late June 1998. Staff began preliminary literature searches on all the exposures to determine the extent of the material that would be available for the review. Several books, journals, and articles were ordered to provide background material for the study. Other types of background information were gathered (e.g., conference abstracts; contact names for individuals involved in veterans health in the government, non-governmental organizations, and veterans groups, and information regarding previous and current Persian Gulf committees).

During the summer months, the staff also began soliciting nominations for the committee to conduct the study. Hundreds of requests for nominations were sent by letter, fax, and phone to a variety of organizations and individuals, including: IOM/NAS members, National Research Council (NRC) and IOM boards and divisions, universities (public and private), government agencies, non-government agencies, veterans groups, medical centers, and schools of public health. Staff conducted bibliographic searches on the research of potential committee members and gathered bios for all individuals nominated for the committee. The long process of contacting hundreds of nominees began in the fall; staff discussed the task with each individual, as well as discussing issues of bias, conflicts of interest, and service on previous Gulf War committees. Many of the individuals that were contacted had to be eliminated from consideration for the following reasons: prior service on other Gulf War committees; research directly related to the topic of the study; or funding (in the form of contracts or grants) from the Department of Veterans Affairs (VA) or the Department of Defense (DoD). Additionally, all government employees were eliminated from consideration. Further, many potential candidates, that met our criteria for service, declined our invitation to serve on the committee for a variety of reasons including prior commitments and their own complicated schedules and heavy workloads.

The committee selection process was further lengthened by the high standards that were set for this particular committee. In addition to the criteria mentioned above, we wanted to be sure that none of the committee members conducted research that was specific to the exposures that would be studied in phase one; however, the committee would have to deliberate and decide which exposures to review in the first phase of the study. Therefore, we put forth a nomination package for a small executive committee of senior researchers and IOM members who were tasked with making the decisions regarding the methodology that would be used to conduct the study, the terminology for the categories of evidence, and the selection of exposures. This small executive committee held two meetings in January and February 1999 (agendas enclosed) and completed their tasks. The methodology and terminology (enclosed) used in the previous Veterans and Agent Orange studies have been adopted for the Gulf War study, with some modification of the terminology. Additionally, the executive committee provided numerous nominations for the full committee.

The small executive committee also determined the exposures that would be studied during phase one. These include: uranium/depleted uranium; nerve agents (sarin and cyclosarin); vaccines (anthrax and botulinum) and the effects of the use of squalene; and pyridostigmine bromide. Additionally, when warranted by the literature, the committee also decided to examine other compounds that may act in synergy with the primary exposures that are being studied, including the role of stress. Although there were several ways in which the committee could have chosen the exposures (e.g., exposures with different types of literature, such as animal, human, or mechanistic data; or based on health effects of interest), they decided that they would consider the exposures of most concern to the veterans (as presented to the committee, during their January and February meetings, by representatives of various veterans' organizations).

The staff immediately began the process of contacting the additional potential committee members and conducting detailed searches on the exposures to be studied in phase one. Staff and committee members reviewed over 10,000 abstracts for a determination of the relevance of the research for this study and the need to order the full text of the articles. The searches were conducted on approximately 21 databases (MEDLINE, Cancerlit, Toxline, HealthSTAR, Health and Wellness DataBase, CAB HEALTH, NTIS, PsycINFO, Enviroline, Environmental Bibliography, International Pharmaceutical Abstracts, Occupational Safety and Health., World TranslationsIndex, Pascal, Life Sciences Collection, BIOSIS PREVIEWS, Dissertation Abstracts

Online, Conference Papers Index, Inside Conferences, EMBASE, and SciSearch). The literature was searched primarily from the early 1960s to the present. For a few compounds (e.g. pyridostigmine bromide), however, we expect to look at the literature from an even earlier time period.

In April, the first meeting of the full committee was held (agenda enclosed). The committee members were briefed on earlier decisions, discussed their task, and heard from numerous individuals representing the government and various veteran communities to provide background for their work. The committee was divided into working groups representative of each exposure to be studied. Each group has at a minimum, an epidemiologist, a toxicologist (immunotoxicologist, neurotoxicologist, heavy metal toxicologist), and a clinician (with the relevant expertise in environmental/occupational medicine, neurology, endocrinology, rheumatology, and immunology). Additionally, the committee has an expert in exposure modeling, psychoneuroimmunology, and clinical psychology.

In addition to providing each new committee member with all the background material that was assembled for the executive committee, all committee members received additional background information, and the detailed results of all the searches that were conducted on the various exposures. The committee members are currently in the process of reviewing the results of the searches so that they may inform staff of additional information that they might require as they analyze the hundreds of articles, reports, and books that they will use to determine the strength of the evidence between exposure and health outcomes or symptoms. To ensure that each committee member is reviewing the material in a uniform manner, summary sheets have been developed and provided to the committee.

The committee will meet again in Washington, DC on June 14-15 and will hear from numerous scientists and researchers that will provide them with additional information about the exposures and mechanisms of interest. There will be a public meeting at the main National Academy of Sciences building, tentatively scheduled for September 16-17, 1999. The final meeting in 1999 will be held in December; however, the dates have not yet been selected. It is anticipated that there will be a meeting in March or April of 2000 to reach agreement on conclusions and recommendations. Following that meeting, final writing assignments will be made and the report will be prepared for review. We anticipate a review during the summer months and printing and release of the report in August 2000.

We have enclosed for your information:

- Statement of Task
- Committee Roster
- Agendas from January, February, and April meetings
- Terminology from Veterans and Agent Orange
- Summary of search results

Please contact us if you have any questions.

cc: Susanne Stoiber
Kathleen Stratton
Cathy Liverman

Statement of Task

Major Unit: IOM
Division, Office or Board: Major Unit: Institute of Medicine
Division: Health Promotion Disease Prevention
Subject Committee: Health Effects Associated with Exposures During Persian Gulf War
Staff Officer Name: Carolyn Fulco, Catharyn Liverman

Statement of Task

The purpose of this project would be to conduct a review of the scientific and medical literature regarding adverse health effects associated with exposures experienced during the Persian Gulf War. The review will include assessments of biologic plausibility that exposures, or synergistic effects of combinations of exposures, are associated with illnesses experienced by Gulf War veterans. The review will include recommendations for additional scientific studies to resolve areas of continued scientific uncertainty related to the health consequences of Gulf War service.

The project will be conducted in three phases. The first phase, addressed in this project, will develop the methods to be used and criteria for inclusion of exposures and health outcomes. The first phase will review the literature regarding some prototypic exposure-health effect relations. The remaining exposures will be the subject of the second phase. The final phase will be a series of updates of the literature and the associations; these updates will be produced every two or three years. Exposures to be considered include, but are not limited to, depleted uranium, pesticides, insecticides, chemical and biological warfare agents, vaccines, pyridostigmine bromide, heat stress, solvents, paints, fuels, smoke from oil-well fires, and sand. Because the data sources for assessing the relation between these exposures and health effects vary greatly in quantity, quality, and applicability to the exposures experiences during the PG war, the review will include directions for future research to resolve continued scientific uncertainty.

Sponsor: Department of Veterans Affairs

Date of Statement: January 13, 1998

INSTITUTE OF MEDICINE
NATIONAL ACADEMY OF SCIENCES
Division of Health Promotion and Disease Prevention

IOM Committee on Health Effects Associated with Exposures Experienced During the Gulf War

COMMITTEE ROSTER

Harold C. Sox, Jr., M.D., *(Chair),*
Professor and Chair, Department of Medicine, Dartmouth-Hitchcock Medical Center

Michael Aschner, Ph.D.
Associate Professor, Department of Physiology and Pharmacology, Wake Forest University School of Medicine

Patricia A. Buffler, Ph.D.
Professor of Epidemiology School of Public Health, University of California at Berkeley

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Firdaus Dhabhar, Ph.D.
Research Associate, The Rockefeller University

Anthony L. Komaroff, M.D.
Professor of Medicine, Harvard Medical School, Editor-in-Chief, Harvard Medical Publications

Janice L. Krupnick, Ph.D.
Professor of Psychiatry, Georgetown University

Herbert Lowndes, Ph.D.
Professor, College of Pharmacy, Rutgers University

Ernest Mazzaferri, M.D.
Professor and Chairman, Department of Internal Medicine, The Ohio State University

Demetrios J. Moschandreas, Ph.D.
Professor of Environmental Engineering, Illinois Institute of Technology

Charles E. Phelps, Ph.D.
Provost, University of Rochester

Samuel J. Potolicchio, M.D.
Professor of Neurology, George Washington University Medical Center

Peter H. Schur, M.D.
Professor of Medicine, Harvard University, Brigham and Women's Hospital

Francoise Seillier-Moiseiwitsch, Ph.D.
Associate Professor of Biostatistics, University of North Carolina School of Public Health

Walter C. Willett, M.D., Dr. P.H.
Professor and Chairman, Department of Nutrition, Harvard School of Public Health

Scott L. Zeger, Ph.D.
Professor and Chair, School of Hygiene and Public Health, Johns Hopkins University

HPDP Board Liaison
Donald Mattison, M.D., M.P.H.
Medical Director, March of Dimes

MFUA Board Liaison
Robert W. Miller, M.D., Dr.P.H.
Scientist Emeritus, National Cancer Institute

INSTITUTE OF MEDICINE

National Academy of Sciences
2101 Constitution Avenue, NW
Washington, DC 20418

Committee on Health Effects Associated with Exposures Experienced During the Persian Gulf War

First Meeting: January 11-12, 1999

REVISED AGENDA

Monday, January 11 – NAS Board Room

EXECUTIVE SESSION

8:30 AM - 9:00 AM	Breakfast	
9:00 AM - 9:15 AM	Introduction of committee and staff	Harold Sox
9:15 AM - 9:30 AM	Brief discussion of the work of the NAS/NRC/IOM	Kathleen Stratton
9:30 AM - 10:15 AM	Bias discussion/conflict of interest	Clyde Behney
10:15 AM - 10:30 AM	Break	

OPEN SESSION

10:30 AM - 11:15 AM	Comments from sponsor and discussion of task	Frances Murphy
11:15 AM - 12:00 PM	Comments from The American Legion	Matthew Puglisi
12:00 PM - 12:15 PM	Comments from the National Gulf War Resource Center	Paul Sullivan

EXECUTIVE SESSION

12:15 PM - 1:00 PM	Lunch	
1:00 PM - 1:30 PM	Discussion of task: origins of the study; current legislation statement of task; expectations of sponsor and other important audiences (e.g., veterans, Congress)	Harold Sox IOM staff
1:30 PM - 2:30 PM	Perspective from previous IOM Committee on PG Health	John Bailar
2:30 PM - 3:30 PM	Discussion of approach and methods used in Agent Orange study	Mike Stoto
3:30 PM - 3:45 PM	Break	
3:45 PM - 6:00 PM	Begin discussion of approach for conduct of study: *consideration of approach, methods, terminology *consider exposures for phase one/rationale *composition for full committee *agree on schedule/timeline *plan for workshop/public meeting(s)	

6:00 PM Reception and Dinner, NAS Executive Dining Room

Tuesday, January 12 -- NAS Board Room

EXECUTIVE SESSION

8:30 AM - 9:00 AM	Breakfast
9:00 AM - 12 noon	Continue discussion of approach for conduct of study: *consideration of approach, methods, terminology *consider exposures for phase one/rationale *composition for full committee *agree on schedule/timeline *plan for workshop/public meeting(s)
12:00 noon - 1:00 PM	Lunch
1:00 PM - 3:00 PM	Finalize plans for next meeting: *agenda items *speakers/groups *names for additional committee members *assignments on rationale for any decisions regarding exposures and methodology/terminology *materials/documents and references needed by committee members

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National Academy of Sciences
Committee on Health Effects Associated with Exposures Experienced During the Persian Gulf War

Second Meeting: February 16, 1999
Cecil and Ida Green Building
2001 Wisconsin Avenue, NW
Washington, D.C.

AGENDA

Tuesday, February 16 -- Green 126 (phone: 202/334-3926)

EXECUTIVE SESSION

8:00 AM - 8:30 AM	Breakfast	
8:30 AM - 8:45 AM	Introduction and Meeting Goals	Harold Sox
8:45 AM - 9:00 AM	Brief Bias Discussion with Dr. Phelps	Susanne Stoiber/Clyde Behney
9:00 AM - 9:45 AM	Begin Discussion of Methodology/Design Issues for Conducting the Study **(Tabs 4 and 5)** • Developing a case definition of Persian Gulf Syndrome (see Hyams paper) • Developing a list of health outcomes • Ensuring standardized decision-making • Conducting the literature search • Categories of evidence for associations	
9:45 AM - 10:00 AM	Break	

OPEN SESSION

10:00 AM - 12:00 PM	Panel Discussion with VA and DoD Physicians **(Tab 3)**	

EXECUTIVE SESSION

12:00 PM - 1:00 PM	Lunch	
1:00 PM - 1:45 PM	Finalize Decision on Exposures **(Tab 2)**	Committee
1:45 PM - 4:00 PM	Continue Discussion of the Methodology/Design Issues **(see above and Tabs 4 & 5)**	Committee
4:00 PM - 4:45 PM	Discussion of Report Outline **(TAB 1)**	Committee
4:45 PM - 5:00 PM	Discussion of Future Meetings • Plans/procedures for April meeting (committee members will meet with working groups, choose exposure) • Plans for June workshop (dates, format, speakers, etc.)	
5:00 PM	Adjourn	

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National Academy of Sciences

Committee on Health Effects Associated with Exposures Experienced During the Persian Gulf War

Third Meeting: April 27-28, 1999
Cecil and Ida Green Building
2001 Wisconsin Avenue, NW
Washington, D.C.

AGENDA

Tuesday, April 27 -- Green 130 (phone: 202/334-3930)

EXECUTIVE SESSION

8:00 AM - 8:30 AM	Breakfast	
8:30 AM - 9:00 AM	Introduction and Meeting Goals	Harold Sox
9:00 AM - 10:15 AM	Bias Discussion	Susanne Stoiber
10:15 AM - 10:30 AM	Break	

OPEN SESSION

10:30 AM - 11:15 AM	Charge to the Committee Fran Murphy, VA
11:15 AM - 12:30 PM	Discussion regarding CDC's work on Gulf War Illness Drue Barrett, CDC
12:30 PM - 1:15 PM	LUNCH
1:15 PM - 2:15 PM	Veterans' Perspective Matt Puglisi, American Legion Paul Sullivan, National Gulf War Resource Center John McNeill and Rick Hirst, Veterans of Foreign Wars
2:15 PM - 3:00 PM	Office of the Special Assistant for Gulf War Illnesses CAPT Michael Kilpatrick

EXECUTIVE SESSION

3:00 PM - 6:00 PM Committee Discussion

- Decisions made by the Executive Committee (exposures and methodology) (TAB 1)
- Statement of Task and Schedule (TAB 1)
- Draft Report Outline (TAB 2)
- Study Process (working groups, score sheets, use of database) (TAB 3)

Wednesday, April 28 -- Green 130 (phone: 202/334-3930)

EXECUTIVE SESSION

8:00 AM - 8:30 AM	Breakfast	
8:30 AM - 8:45 AM	Remarks from IOM President	Kenneth Shine
8:45 AM - 9:00 AM	Remarks from the Director of the IOM Medical Follow-up Agency (MFUA)	Richard Miller
9:00 AM - 9:15 AM	Goals for the working groups • Develop a plan of work (use of score sheets, databases, list of health outcomes) and schedule (dates/location for working group meetings) • Review draft outline (Tab 2) • Assignments • Speakers/topics for June scientific workshop • Other materials needed	Harold Sox
9:15 AM - 11:00 AM	Working group meetings (Tab 4)	
11:00 AM - 12:30 PM	Reports from the working groups	
12:30 PM - 1:30 PM	Lunch	

1:30 PM - 3:00 PM	Committee Discussion
	• Overall plan of work
	• Final schedule of work
	• Revise draft report outline
	• Plan for June scientific workshop (June 14-15th)
	• Future meetings
	  • Working group meetings
	  • September 16th and 17th
	  • December or January
	  • March or early April
	• Writing assignments	

3:00 PM	Adjourn	

nportant to the overall review. Ultimately, the conclusions expressed in iis report about causation are based on the committee's collective judg- ıent. The committee endeavored to express its judgments as clearly and recisely as the available data allowed.

SUMMARY OF THE EVIDENCE

The committee's specific mandate was to determine, if possible,

1. whether there is a statistical association between the suspect diseases ıd herbicide use, by taking into account the strength of the scientific evi- ence and the appropriateness of the methods used to detect the association;
2. the increased risk of disease among individuals exposed to herbi- des during service in Vietnam; and
3. whether there is a plausible biologic mechanism or other evidence of causal relationship between herbicide exposure and a disease.

The committee addressed the first part of this charge by categorizing ch of the health outcomes under study into one of the four categories scribed below on the basis of the epidemiologic evidence that it reviewed. onsiderations of biologic plausibility did not enter into the committee's cision about how to categorize these outcomes, but plausibility is dis- ssed separately after the assessment of the epidemiologic evidence. The estion of increased risk in Vietnam veterans is also addressed for each alth outcome, subject to the considerations discussed below.

Categories of Association

The categories used by the committee were adapted from those used by International Agency for Research on Cancer in evaluating the evidence carcinogenicity of various agents (IARC, 1977). Consistent with the ırge to the Secretary of Veterans Affairs in P.L. 102-4 (which is stated in ms of statistical association rather than causality) the distinctions be- een the categories are based on "statistical association," not on causality is common in scientific reviews. The distinctions reflect the committee's lgment that a statistical association would be found in a large, well- ;igned epidemiologic study of the outcome in question in which exposure herbicides or dioxin was sufficiently high, well-characterized, and appro- ately measured on an individual basis.

- *Sufficient Evidence of an Association*: Evidence is sufficient to con- de that there is a positive association. That is, a positive association has n observed between herbicides and the outcome in studies in which ınce, bias, and confounding could be ruled out with reasonable confi-

dence. For example, if several small studies that are free from bias and confounding show an association that is consistent in magnitude and direction, there may be sufficient evidence for an association.

- *Limited/Suggestive Evidence of an Association*: Evidence is suggestive of an association between herbicides and the outcome but is limited because chance, bias, and confounding could not be ruled out with confidence. For example, at least one high quality study shows a positive association, but the results of other studies are inconsistent.
- *Inadequate/Insufficient Evidence to Determine Whether an Association Exists*: The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an association. For example, studies fail to control for confounding, have inadequate exposure assessment, or fail to address latency.
- *Limited/Suggestive Evidence of No Association*: There are several adequate studies covering the full range of levels of exposure that human beings are known to encounter, that are mutually consistent in not showing a positive association between exposure to herbicides and the outcome at any level of exposure. A conclusion of "no association" is inevitably limited to the conditions, level of exposure, and length of observation covered by the available studies. In addition, the possibility of a very small elevation in risk at the levels of exposure studied can never be excluded.

Increased Risk in Vietnam Veterans

The categories related to the association between exposure to chemicals and health outcomes, not to the likelihood that any individual's health problem is associated with or caused by the herbicides in question. As stated early in this chapter, the most desirable evidence as a basis for answering this type of question involves knowledge of the rate of occurrence of the event in those Vietnam veterans who were actually exposed to herbicides, the rate in those who were not exposed (the "background" rate of the event in the population of Vietnam veterans), and the degree to which any other differences between exposed and unexposed groups of veterans influence the difference in rates. When those Vietnam veterans who are actually exposed have not been properly identified, as has generally been the case in existing studies, this question becomes difficult to answer. Although there have been numerous health studies of American and other Vietnam veterans, most have been hampered by relatively poor measures of exposure to herbicides and/or dioxin and other methodological problems. Indeed, most of the evidence on which the findings in this report are based comes from studies of people exposed to dioxin or herbicides in occupational and environmental settings rather than from studies of Vietnam veterans.

The committee found the available evidence sufficient for drawing con-

Search of Online Databases--SUMMARY

Databases Searched for DU, PB, Sarin, Vaccines, and Gulf War:

File 155:MEDLINE(R) 1966-1999/Apr W3
File 156:Toxline(R) 1965-1998/Dec
File 159:Cancerlit 1975-1999/Feb
File 151:HealthSTAR 1975-1998/Dec
File 162:CAB HEALTH 1983-1999/Jan
File 73:EMBASE 1974-1999/Feb W2
File 6:NTIS 64-1999/Apr W1
File 11:PsycINFO(R) 1967-1998/Dec
File 40:Enviroline(R) 1975-1998/Oct
File 68:Env.Bib. 1974-1999/Mar
File 5:BIOSIS PREVIEWS(R) 1969-1999/Mar W1
File 74:Int.Pharm.Abs. 1970-1999/Feb
File 161:Occ.Saf.& Hth. 1973-1998/Q3
File 295:World Transl.Index 1979-1997/Dec
File 144:Pascal 1973-1999/Jan
File 76:Life Sciences Collection 1982-1999/Jan
File 77:Conference Papers Index 1973-1999/Mar
File 65:Inside Conferences 1993-1999/Mar W1
File 149:IAC(SM)Health&Wellness DB(SM) 1976-1999/Mar W1
File 35:Dissertation Abstracts Online 1861-1999/Mar
File 34:SciSearch(R) Cited Ref Sci 1990-1999/Feb W4
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec

Total unique items from searches:

DU	4846
PB	2531
Sarin	1634
Vaccines	1490
Gulf War	743
TOTAL ITEMS	**11,244**